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JANUARY 1st, 1943.

No. 4

SECOND PRIZES

It is from Plutarch that we learn the comment of Antisthenes when people told him that one Isemenias was an excellent piper. "It may be so," said he, "but he is but a wretched human being, otherwise he would not have been an excellent piper." We find also that King Philip told his son Alexander, who had just played a piece of music charmingly and skillfully at a merry-meeting; "Are you not ashamed, son, to play so well?" In other words in the opinion of these judges one does not merit awards for an accomplishment that one performs naturally by virtue of a divine gift. It is the success gained against ill-fate, ignorance and perversity that deserves reward.

The British people possess certain qualities which they inherit from nature, breed by tradition and bear in a monstrous climate, and which have borne them through many catastrophes and will see them through many more. They are notorious for understatement and a phlegmatic outlook. They possess initiative, skill in getting out of tight corners and because of their fanatical love of sport they can take defeat and victory with the equanimity they both deserve. In these respects they take the first prizes.

It is said that to win the first prizes luck and judgment are essential, while second prizes can be obtained merely by hard work. When the Allies are victorious they will hold the fate of the world in their hands. But they will not be the first to achieve the distinction of being masters of the civilised world. In the past great nations passed away because of internal strife and a badly organised social system. In the future it will be necessary for each country to determine new home and foreign policies to live in this changed world, and in neither category has Britain shone of late. On their success depends the length of time that Britain will remain in the forefront of the Allies.

"Your sons and your daughters shall prophesy, your old men shall dream dreams, your young men shall see visions," so run the gracious promises foretold by the prophet Joel. Yet our young men have not been moved to prophesy or to see visions. They have been

utterly frank in their contempt of the past order of things and not a little cynical of those who attempt to alter them. To those who have read Richard Hillary's book, The Last Enemy, will come a clearer understanding of the modern youth of a certain class, yet, under the present scheme, still the future ruling class. "Before the war we were disillusioned and spoiled, and referred to by the press as the Lost Generation. We looked for little more than experience in a world that was rapidly disintegrating." war became their opportunity for self-realisation, for development of the individual, and for demonstrating dislike of organised emotion and patriotism. But as truth proverbially hovers on the lips of dying men, so youth may sense disaster before the old dare act and frame their philosophy accordingly.

Our old men are dreaming dreams; one is unable to open a newspaper or a periodical without reading the dreams of the great personages of the land. In written and spoken words their fanciful pictures of the future are spread across the world. But at last, after three years of decrying the enemy's New Order we have found a man to whom we can be grateful. In reply to the mass murder, pillage and desecration of sacred objects of art and religion Sir William Beverdige has given answer, and for that alone he merits the highest praise. Since President Roosevelt set out the Four Freedoms the phrase "freedom from want" merely denoted a hope. Now it has been turned into an attainable object of national endeavour. The Report has received the publicity and the prominence it needed and richly deserved. The duty of every citizen is to examine it; the duty of doctors to examine it is even greater for it enters into their sphere of activity. The Report provides for free medical treatment for all, and hazards some suggestions for the reorganisation of medical services.

It is imperative that these dreams be examined carefully and fairly, for on them depends the making of our future. To win the war is to merit the second prize, but we must go beyond that, we must invoke luck and exercise judgment to win the first prize.

A NOTE ON THE RH FACTOR AND ITS SIGNIFICANCE

By H. F. BREWER

Recent work by Landsteiner and Levine has demonstrated the presence of another antigenic component in the human red cell termed the rhesus factor, or, for brevity, the Rh factor. Its discovery depended on the finding that the serum of a rabbit which had been inoculated with the red cells of a rhesus monkey developed the property of agglutinating the red cells of most, but not all, human subjects irrespective of their ordinary A, B, O grouping. Results showed that in a sample of the general population approximately 85% of people contained this Rh factor in their red cells whilst in the remaining 15% it was absent, the cells not being agglutinable by the specific anti-Rh serum. The latter are referred to as Rh-negative individuals and the former as Rh-positive. Experience in forming a panel of Rh-negative donors at the Luton Blood Depot is in accord with these figures.

There is no naturally occurring anti-Rh agglutinin corresponding to the a (anti-A) and β (anti-B) iso-agglutinins of the A, B, O system in human sera, but the importance of the Rh antigen lies in the fact that it is capable under certain conditions in man of stimulating the production of an anti-Rh agglutinin. These conditions are first and foremost when an Rhnegative mother becomes pregnant with an Rhpositive embryo, and, secondly, when an Rhnegative patient has one or more transfusions with Rh-positive blood. The recognition of the Rh factor and its corresponding anti-body is essential in transfusion therapy since the introduction of Rh-positive blood into a recipient whose serum contains anti-Rh agglutinins may result in a hæmolytic reaction varying from a mild to a fatal grade.

MATERNAL IMMUNISATION TO THE RH FACTOR AND ITS ROLE IN ERYTHROBLASTOSIS FŒTALIS

It has been shown by Levine and his coworkers in the United States and confirmed by Boorman, Dodd and Mollison in this country that the combination of an Rh-negative mother pregnant with an Rh-positive baby (the Rh factor being derived from the father as a Mendelian dominant) is prone to be associated with the development in the child of erythroblastosis fœtalis. The manifestations of the latter are various and comprise hydrops fœtalis, congenital anæmia of the new born, icterus gravis (the milder types fuse imperceptibly with

so-called physiological jaundice) and a succession of still births unrelated to any of the known causes. The characteristic combination of Rh-negative mother and Rh-positive child in this affliction led Levine to put forward his theory of the causation of the condition. His thesis is that the mother becomes immunised to the Rh factor present in the red cells of her developing fœtus and that the Rh anti-body (identified as the anti-Rh agglutinin) diffuses across the placenta into the fœtal circulation and exerts a destructive influence on its red cells. This is a fascinating and logical explanation. That a progressive immune response is involved is further suggested by the fact that often the first child is unaffected in a series of subsequent cases. Other factors must, however, play a part for the occurrence of babies with erythroblastosis only results in about 1 in 10 pregnancies in which this Rh distribution is present and the stage set. In the remainder the mother may fail to react to the antigen or the Rh anti-body may not succeed in passing across the placenta. A few examples of erythroblastosis fætalis have been recorded in which the Rh factor cannot be incriminated (mother and child both being Rh-positive or both Rh-negative); in some of these the combination has been such on the A, B, O system that the iso-agglutinin $(a \text{ or } \beta)$ present in the mother's blood was incompatible with the agglutinogen (A or B) in the infant's erythrocytes-e.g. a Group O mother with a Group A child. It is, of course, extremely rare for such a common combination (the Rh factor being excluded) to be associated with erythroblastosis of the infant and the additional cause in cases of this nature is still a matter of speculation. At the Luton Depot to date of fivemothers investigated with a history of erythroblastosis babies all were Rh-negative. In only one were potent anti-Rh agglutinins present but the interval after the last pregnancy varied up to 12 months.

IMMUNISATION APART FROM PREGNANCY

Transfusion of any Rh-negative individual with A, B, O compatible but Rh-positive blood, may evoke the formation of anti-Rh agglutinins in the recipient. This is especially likely to occur in any condition (e.g. aplastic anæmia) in which a succession of transfusions is frequently necessary. If these are provided

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by one Rh-positive donor or if the majority of various donors taken are Rh-positive a progressive increase of anti-Rh agglutinin titre in the patient's blood is likely to result.

RECOGNITION OF RH FACTOR

Anti-Rh grouping sera is mainly derived from the blood of Rh-negative mothers who have recently or in the past had one or more infants affected with erythroblastosis. The range of titre of the anti-Rh agglutinins is lower than that of the α and β iso-agglutinins of the A, B, O system and maximum titres do not compare with those found with the latter. The sera of a considerable number of mothers may have to be examined before one of satisfactory potency (titre of anti-Rh agglutinin, 1 in 64 or above) is found. Titre is said to be highest 2 or 3 weeks after parturition but it may remain at a high level for several years after delivery. At the Luton Depot the most potent serum (titre, 1 in 128) was obtained from a mother who gave birth to an erythroblastotic child 5 months earlier. The small supply of good grouping serum available is a limitation to work on the subject. Unless the serum is group AB, elimination of the a or β iso-agglutinin or both must be carried out by absorption with Rh-negative homologous cells in order to render the serum suitable for all cells of the A, B, O system.

In testing for the presence of the Rh factor in erythrocytes a tube technique based on that recommended by Landsteiner and Wiener is essential; the tile or opal glass plate method so frequently employed in ordinary grouping is not satisfactory. Equal parts (approximately 0.05 c.c.) of the specific anti-Rh serum and a 1-2% saline suspension of the unknown cells are added to a small 2in. x 1/4in. tube and mixed. Known Rh-positive and Rh-negative red cells are put up in similar manner as controls. The tubes are placed in an incubator for 2 hours at 37° C., as advised by Levine, and then read. The sedimented red cells at the bottom of the tube have a characteristic appearance according as to whether they are Rh-positive or Rhnegative; with the latter the sediment has a typical smooth surface and regular margin, and with the former a wrinkled surface and serrated margin. Confirmation as to the presence or absence of agglutination is obtained by transferring a drop of the red cell sediment as gently as possible to a microscope slide with a Pasteur pipette and examining for agglutinates under the low power of the microscope. It is advisable to regard no cells as Rh-negative unless tested against 3 known different potent anti-Rh In testing an unknown serum for the presence of anti-Rh agglutinin the serum should be put up as above with a series of 15-20 Group O cells and with 2 known Rhpositive and 2 known Rh-negative Group O cells. If agglutination occurs with the positive controls and also with the majority of the Group O cells but not with the negative controls the presence of anti-Rh agglutinins can be assumed. Estimation of titre of the anti-Rh agglutinins, when present, is performed by putting up the serum in the manner described in serial dilutions with known Rh-positive cells and noting the highest dilution in which agglutination can be observed.

For the direct matching test between proposed donor's cells and patient's serum to eliminate the risk of anti-Rh agglutinins in the latter reacting with Rh-positive transfused cells the same tube technique is employed. A weak saline suspension of the donor's blood is mixed with an equal part (approximately 0.05 c.c.) of the recipient's serum in one of the standard small tubes and the reaction read after 2 hours in the incubator at 37° C. The cell sediment at the bottom of the tube is looked at naked eye and the impression as to whether the result is positive or negative confirmed by removing a little of it with a Pasteur pipette, placing on a slide as gently as possible and examining under the low power of the microscope. If the slightest suggestion of agglutinates be present this particular donor should be rejected. Taylor and Race have pointed out the advisability of using a titration method especially in the direct matching test since some sera containing anti-Rh agglutinins may exhibit a prozone phenomenon; with the latter agglutination may be weak or absent in low dilutions of the serum although very definite in the higher.

In all these tests it is necessary to remove as a preliminary the a and β iso-agglutinins from the serum by absorption if there is any likelihood of their reacting with A or B agglutinogens in the cells to be tested. The necessity for full controls with known Rhpositive and Rh-negative cells cannot be over emphasized and the possibility of rouleaux formation and auto-agglutination must be guarded against. The technique for the recognition of the Rh factor contains numerous potential pitfalls and reliable interpretation of results can only be obtained with considerable experience and practice.

PRACTICAL IMPLICATIONS

A mother who has given birth to a child affected with erythroblastosis in any of its

various manifestations, or who gives a history of previous infants with this disease is almost certainly Rh-negative and there is a strong probability of her serum containing anti-Rh agglutinins in appreciable concentration at the end of the pregnancy and for some time (possibly years) afterwards. In the event of a transfusion being required Rh-negative blood of suitable A, B, O group is essential. The husband's blood is Rh-positive (being responsible for this factor in the child) and is particularly contra-indicated. In situations of urgency and until known Rh-negative blood is available the use of plasma or serum is advised. Only in an exsanguinated mother of this type is the risk of transfusing Rh-positive blood (85% of donors) justifiable.

In women who have a past history of infants with erythroblastosis and who have again become pregnant, demonstration of the presence of anti-Rh agglutinins in their blood during the latter part of the pregnancy should point to the advisability of having suitable Rh-negative blood available in advance, in case transfusion should be required at some later stage of the pregnancy.

In infants affected with erythroblastosis it has shown that Rh-negative transfused erythrocytes have in most cases a longer survival rate than Rh-positive ones. This is dependent on the prolonged passage into the infant of anti-Rh agglutinins prior to birth from the maternal circulation. Accordingly when transfusing these babies Rh-negative blood is preferable; in case of urgency Rh-positive blood may be used.

Rh-negative patients of either sex may produce anti-Rh agglutinins following the transfusion of Rh-positive blood, compatible according to the A, B, O grouping. This response is particularly liable to occur after a succession of transfusions with donors unselected as regards the Rh factor. The result may be a frank hæmolytic reaction after one of the later transfusions or more frequently the transfusion does not produce the anticipated red cell and hæmoglobin rise in the patient. In the latter case there is a slow break-up and elimination of the transfused cells which may be unrecognised in the absence of any clinical signs of

hæmolysis. Sometimes no immediate reaction is apparent but the patient commences to pass little or no urine after the transfusion and slowly develops uræmia. Any of these features in a patient who has had two or more transfusions should lead to a suspicion of an Rh incompatibility provided the A, B, O grouping is correct. Also, the serum of any Rh-negative recipient who has been previously transfused should be examined for the presence of anti-Rh agglutinins and only Rh-negative blood used if they are demonstrated.

The ideal procedure in blood transfusion would be always to give Rh-negative blood to Rh-negative recipients but the technical features involved, particularly the difficulty of obtaining adequate amounts of potent anti-Rh grouping sera, render this impracticable at the present time. In cases in which an Rh incompatibility reaction is a possibility the direct matching test should include the special tube technique previously described.

Lastly, the Rh factor may be used to support the diagnosis of erythroblastosis fætalis. Demonstration that the infant is Rh-positive, the mother Rh-negative (especially if there are anti-Rh agglutinins in her serum) is strong confirmatory evidence. Absence of these findings does not exclude the diagnosis but it makes it very unlikely.

The writer is very grateful to Drs. G. L. Taylor and R. R. Race of the Galton Laboratory, Cambridge, for advice on the technical aspect, and also for confirming early results. Both to them and to Dr. P. L. Mollison of the S.W. London Blood Supply Depot he is indebted for intial samples of anti-Rh grouping sera. Mr. R. Hudson, senior laboratory assistant at the Luton Depot, has ably collaborated in the technical work.

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ABERNETHIAN SOCIETY

The Society held its last meeting of the year on Thursday, November 26th, to debate the motion that "this House approves the admission of women students to this medical college." Dr. Scowen was in the chair and opened the debate with a brief history of the little association Bart.'s had had with women. He then introduced the proposers, Mr. Bedford Russell and Dr. Harold, and the opposers, Mr. Vick and Mr. Harmer.

and Mr. Harmer. Mr. Bedford Russell frankly declared that he liked women and he approved of the idea of their entering the College because the platonic friendships as formed between men and women in the American Universities were so charming to him. He then proceeded to a short review of the relations between man and woman: he postulated that the absence of the navel in Adam and Eve was a point in favour of their original equality. Both Adam and Eve were vegetarians, and, as far as contemporary chronicles related, they both indulged in the same simple pastimes for relaxation. But some thousands of years later man had become a predatory athlete while woman stayed at home roaming the cave thinking of the future of her offspring. He said that the emancipation of woman dated from the introduction of the velocipede and the invention of freer clothing suited to that activity. He had stories to tell of the bachelor girls at the Universities and remembered when the students of a London Hospital requested that the women students should not be allowed to compete for prizes, since they always won them. But nowadays men and women were on an equal basis and there was no need for condolences for a father on the birth of a fourth daughter. Women had progressed far in their evolution, and some might even be said to have a soul. He then proposed that man really knew nothing about woman, and that she had now earned a recognition that had hitherto been withheld. Team spirit, he suggested, may have brought women to trust each other. He thought that the introduction of women students to the College should be gradual and that five of the best from the three great Universities should be the first. But, and here Mr. Bedford Russell was very insistent, there should be separate changing rooms. Man, he concluded, was no longer of any use to woman since she now had her latch-key and could earn her own keep.

Dr. Harold seconded the proposition, saying that he would be short like ladies' skirts and cover the most important points. Having admitted women to medicine, he argued, they should now be given equal education How could criticism of their efforts be levelled at them when they had not had equal chances of demonstrating their ability. Women had fulfilled all that had been expected of them in the past, and there was a great deal they could do, and would do in the future. Medicine was becoming increasingly specialised and there was no longer the need for the hard-riding county physician and the swashbuckling surgeon. Child welfare, health clinics and routine work were becoming increasingly important and women were well fitted for these posts. The State was having an increasing effect on the profession, and there were going to be many more state-aided students after the war. The Army of Occupation would need hundreds of men and therefore the State would see that there were greater numbers of doctors, both men and women. Let the Hospital act first and open its gates voluntarily and not be dragged in by the State. He asked his audience to notice that the opposition would depend on two major points in their arguments, namely; misogynism and prejudice. Women were said to be a distraction to men at work; Dr. Harold advised his audience to fear nothing. In the matter of prejudice he said that such weak arguments as the lack of cloak-room accommodation would not deter the women. The threat of constipation would not stop feminine progress. After congratulating the house on its healthy and robust appearance he asked it not to sit cross-legged vegetating by the river of progress, but to mount and ride far ahead of the field of prejudice.

The Chairman though it wise at this juncture to remind the House that the opinions expressed by the speakers in no way represented the views of the Hospital authorities or those of the speakers themselves.

Mr. Vick rose with alacrity to oppose the motion, which he thought specious and immoral. He was horrified at the thought of the great mother Hospital, who had given birth to so many fine sons, now having a daughter. As for the opposition, Mr. Bedford Russell, he had always suspected as a revolutionary, for he had occasion to correct him as a student for

writing "wound O.K." in a case history. Dr. Harold had been one of his most brilliant dressers, but he ought to have suspected his duplicity, for Dr. Harold had a fast car and a fast mind and went far ahead of anything necessary at the moment. What was the use of introducing more women to the profession when the majority of men and women patients did not want it. Man has a right to allow whom he likes to handle him. It must be a rara avis, in fact a damn queer avis, who preferred a woman doctor. Welfare and research were important, and so was routine work, but women were not keen on them. Mr. Vick then gave a detailed description of the eight women who worked under him in a Medical Unit during the Great War. They made a sorry collection from women almost out of Jane Austen to one that wrote such enormous amounts of notes of "very very" " awfully awfully " that she ended by bewildering herself. He showed that there was plenty of room for women to work in the provinces. At Oxford University the women students remained at Oxford for their clinical work-a very good thing in his opinion. But the most telling reason against having women in this College was that they simply were not wanted. This was our medical school and as far as we were concerned it was the best. It was built by men for men. It might be fun to have women with their rippling laughter pervading the corridors, but in his experience medical women did not ripple at all. He agreed that co-education was good for girls who had no brothers, so that they could find out the worth of men. If women were admitted to the College, and it would be against the desire of the nurses and sisters, there would have to be a female dean, for discipline among women could only be conducted by a woman. He invited the House to look more closely at the Dean and notice that he had been wasting of late with the thought of this invasion of his sanctuary. Mr. Vick concluded with the statement that in spite of modern trends tradition was everything, loyalty to tradition was strength. It was purely a misguided sense of gallantry that had proposed this innovation. Certainly let there be schools for women, but leave Bart,'s alone.

Mr. Harmer seconded the opposition by contending that the proposition had entirely failed in their arguments. There was decidedly an essential difference between man and woman. The arrival of women in great numbers into the medical profession was by no means inevitable as the profession had suggested. What a horrible thought to imagine oneself one of the first few to arrive here as Mr. Bedford Russell had proposed. He pointed out that Mr. Bedford Russell had been undecided in the middle of his argument as to whose side he was actually on, while Dr. Harold had kissed the Blarney Stone in his youth which might account for his being blown up with his own verbosity. Mr. Vick, on the other hand, had been incredibly convincing. Statistics and personal appearances were all against the proposition. If women were not going to make good doctors there was certainly no place for them here. And if they were good there was no place for them either as Mr. Vick had shown. Women have their privileges and so there was no reason why men should not. Not even the Chairman was impartial, imagine Dr. Scowen with a female Houseman. Mr. Harmer recalled another debate where Dr. Geoffrey Evans had lamented with tears that home life was breaking up in modern times, and that family prayers lead to regularity of habits. Woman's place was by the fireside, said Mr. Harmer, and concluded with an apt quotation from A. G. McDonell.

The debate was then opened to the House and many availed themselves of the opportunity of attacking the undefended fair sex. Mr. Watson brought Nietzsche and the multicoloured appearance of female limbs to make his argument the more convincing. He deplored the inevitable decline in the standard of conversation at luncheon that would follow their admission. Mr. Newbold told the House that he was against the motion in case he became inarticulate before he finished. He had to be careful what he said for his wife was a doctor, but he pointed out that the greatest work had been accomplished in celibacy, and that Rahere himself had come of such a sect. Mr. Roberts suspected that women were using the war as an excuse to go one higher than they need. Mr. Bailey maintained that if women were paid the same as men, women would soon cease to be employed. Mr. Chambers saw horrible visions of a Hogarthian Vicarage of the future and feared many of the Chiefs might be susceptible to Coty. Mr. Leverton rose with trepidation to support the motion, reminding the House that the great work women had done in the Services entitled them to more general consideration; let women be admitted to Bart.'s for the war only. Mr. Headley, being a seeker of truth in the low places of the world, wished y

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the introduction of women for further continuation of his researches. Mr. Whitfield quoted an experience of his while working under a woman doctor when complete chaos had overtaken a delivery on his noticing the doctor had a ladder in her stocking and she was aware that he had noticed it. The Chairman then quickly cleared up a few of the points that had arisen during the debate and on being put to the vote the motion was defeated by 73 votes to 11. The Chairman then adjourned the meeting, having thanked all those who had made it possible.

THE PARKES-WEBER SYNDROME HAEMANGIECTATIC HYPERTROPHY OF LIMBS

By PETER P. REICHENHEIM

The syndrome of hæmangiectatic hypertrophy of limbs, though uncommon, has recently been shown by American workers to be less rare than was previously supposed. Although several cases were reported in the second half of the last century, first by Letenneur in 1859, the condition was comparatively unknown until Dr. F. Parkes-Weber drew attention to it in a paper in 1907. He reported on a case of a female child, twelve weeks old, whose left side was covered with diffuse capillary cutaneous nævi; there was also a small cavernous hæmangioma in the left groin and a prominent dilated vein in the front of the trunk. The left upper and lower limbs were bigger than the right, but there was no difference in length. In a second paper in 1918 he reported on 14 cases which he had collected from the literature. He stated that the tumour-like hæmangiomatous overgrowth of arteries and veins, or "Genuine Diffuse Phlebarteriectasis," is quite distinct from the well-known traumatic arterio-venous aneurysms, as was first shown by Karl Otto Weber, reporting on a case of Krause in 1861. This was in a man aged 33, who had noticed a vascular tumour in the palm of the left hand since he was eight, increasing in size until it finally involved hand and forearm, causing intense pain, atrophy of the fingers and length-ening of the left extremity. The arm had to be amputated and showed abnormal communications between arteries and veins. Parkes-Weber also differentiated between phlebarteriectasis and phlebectasis or so-called congenital varicose veins, in which the veins only are hypertrophied. He mentions a case of Bockenheimer, in which there was extreme dilatation of the veins of the left arm, while the arteries showed only slight sclerotic changes. There was no abnormal communication between arteries and veins and the left humerus was 1 cm.

longer than the right.

Hæmangiectatic hypertrophy of limbs can be distinguished from congenital trophædema, which tends to run in families as described by Milroy and Meige, by the associated vascular abnormalities and the usual increase in length of bones. It can be distinguished from true local gigantism by less-marked hypertrophy and by the associated vascular abnormalities.

There have been also a number of cases of hemi-hypertrophy in association with angiomatous formations. Earlier cases were described by Arnheim and Kalischer, the latter reporting on a 3½-months-old child with right-sided hemihypertrophy associated with angioma formations. A very interesting case was described by Luigi Cagiati in 1907. There was a left-sided hemi-hypertrophy, unilateral enlargement of the veins and arteries, and unilateral hypertrophy of the viscera, which he attributed to the vascular overgrowth. Histologically it was found that the media of the arteries and the media and adventitia of the veins on the affected side were extensively hypertrophied. In recent times Downing has described a case of hemi-hypertrophy of the left side of the body in a man aged 34 associated with a large nævus and varicose veins in the left leg. Terence East's case of "Hemi-Hypertrophy and Cutaneous Telangiectasis" showed enlargement of the right arm and leg only, and should therefore be better classified as a case of hæmangiectatic hypertrophy of limbs. A possibly unique case of congenital phlebarteriectasis associated with coarctation of the aorta was described by

In France the syndrome of hæmangiectatic hypertrophy of limbs is often called after Klippel and Trénaunay, who described it in the beginning of the century.

A case of the Parkes-Weber syndrome is now

described in a boy who has recently been at Friern Hospital.

CASE HISTORY

S. H., a boy of 13, was admitted to Friern Hospital on the 17th July, 1942, under the care of Dr. James Maxwell, complaining of lumps in his right leg. Since birth it had been noticed that his right arm and leg were bigger than the left and that the right side of the body except the face and neck showed bluish-red discolourations. He had always limped slightly on account of his right leg, but otherwise has been quite well; he went to school where he was not handicapped by his deformities, but did not play games, his right leg being too weak for running over long distances.

His mother stated that his birth was normal. He weighed 10 pounds, and was breast fed until he was 8 months old. His development had been normal, he sat up at 6 months, cut his first tooth at 7 months and walked when 14 months old.

Three weeks ago his mother noticed three soft bluish lumps in front of his right shin. As the boy did not feel very well she saw a doctor, who sent him to St. Bartholomew's Hospital. He has been an out-patient of St. Bartholomew's Hospital since his birth for the investigation of his deformities. He has had childish ailments in the past. There have been no deformities in any other member of his family.

Examination on the 18th July, 1942, showed that he was a bright, intelligent, well-developed boy; weight, 7 stones 6 pounds; height, 60 inches.

There was no abnormality in his face and neck except a slight paresis of his right inferior oblique muscle. His visual fields and fundi were normal, and his teeth in good condition.

His chest appeared asymmetrical owing to a bulging of the left side, but on palpation it was found that the bony framework of the thorax was perfectly symmetrical and that the bulging was due to a diffuse soft subcutaneous lipoma which was found situated over the left costal margin. In addition there was one in the left axilla and one overlying the spines of the upper thoracic vertebrae. There was no deformity of the spine. The lungs were normal. The heart was not enlarged, and the

heartsounds normal, no added sounds being heard. The pulse was 70, regular and of normal volume and tension. Nothing abnormal was discovered in the abdomen.

A large bluish-red nævus was situated in the left axilla extending on to the left arm and backwards over the left scapular region crossing the midline at several points. A second nævus of similar colour was situated on the right side of the abdomen below the umbilicus extending into the right leg and ending abruptly at the midline of the body.

The right arm was larger than the left. The increase in size was especially marked in the right forearm and hand. Irregular, diffuse bluish-red navi covered most of the right upper extremity. No enlarged veins were seen. On palpation it was noticed that the right arm was distinctly warmer than the left. It was also found that the increase in size was chiefly due to the increased bulk of the soft tissues and not to skeletal overgrowth. No abnormal pulsations or thrills could be felt over the vessels and no bruits could be heard. The right hand was very much enlarged, especially transversely. This was chiefly due to subcutaneous fatty tumours over the thenar and hypothenar eminences. While the thumbs, index, and middle fingers on both sides appeared to be equal in length, the right ring and little fingers were enlarged. Tone, range of movements, reflexes and sensations were the same on both sides, but in spite of the fact that the patient stated that he was left-handed, his right arm was distinctly more powerful. It will be seen from the accompanying table that, while there was considerable increase in the size of the right limb, there was no appreciable increase in length and that the blood pressures on the two sides were approximately equal. On compressing the brachial artery in the right upper arm by a Riva Roeci cuff no slowing of the heart was observed. (Bradycardiac reaction, see later.) There was no clubbing of the fingers. The patient stated was no clubbing of the fingers. The patient stated that the nails of the fingers of his right hand grew appreciably quicker than those on the left.

The right lower extremity appeared to be bigger, but a little shorter than the left. The increase in size was especially marked in the right leg and foot. The skin of the right leg was of a dusky-bluish colour and a large bluish-red nævus covered most





of the right thigh, leg and foot. Prominent veins were seen ascending chiefly on the medial side of the right leg and thigh. On palpation no difference in temperature between the two legs could be noted. It was even more obvious than in the arms that the increase in size was chiefly due to an increase in bulk of the soft tissues. The bones of the right foot, however, seemed to be bigger than those of the left. Owing to the increase in size of the tissues arterial pulsation over the right femoral, popliteal, dorsalis pedis and posterior tibial arteries was only felt with difficulty. While the patient was lying in bed, no lumps could be seen or felt in front of the right tibia. After he had walked for a few minutes, one could observe four round bluish-purple lumps lying more or less in a row, just lateral to the anterior border of the right tibia. They were all situated in the subcutaneous tissues and were soft and fluctuant. The largest, about one inch in diameter, was overlying a deep notch which could be felt on the anterior border of the tibia about 4 inches below its upper end. When the patient's leg was elevated the lumps disappeared. They were presumed to be cavernous hæmangiomata. Tone, range of movements, reflexes and sensations were the same in both legs. The blood pressure in both legs was about equal, and there was no bradycardiac reaction on compressing the right femoral artery. Urine and bloodcount were normal.

The X-rays showed no abnormalities except in the right arm and leg. While the soft tissues were shown to be enlarged in bulk there was no appreciable enlargement of the long bones in the right arm and leg. The density and structure of the bones was the same on both sides. The bones of the right hand and feet, especially the phalanges of the right ring and little finger showed a uniform enlargement but normal structure and density. A six foot X-ray of the heart showed a normal shadow.

Measurements to	Right Arm	
Tip of acromium to lateral epicon- dyle of humerus Lateral epicondyle humerus to	10"	10"
styloid proc. radius	$9\frac{1}{2}''$	91"
Circumference at junction upper middle third upper arm	$9\frac{1}{2}''$	$8\frac{1}{2}''$
Circumference at junction upper middle third forearm	$10\frac{1}{2}''$	81"
Styloid process ulna to head middle metacarpal	4"	31/2"
Circumference of hand round heads of metacarpels	$9\frac{1}{4}$ $4\frac{1}{4}$ $3\frac{1}{2}$ $110/77$	$6\frac{1}{2}$ $3\frac{1}{2}$ $2\frac{1}{2}$ $108/80$
Measurements	Right Leg	Left Leg
Anterior superior iliac spine to medial mallcolus Medial epicondyle of tiba to medial	331/2"	34"
malleolus Circumference at middle of thigh	16" 15 <u>1</u> "	16" 15"
Circumference at middle of leg Length of foot Circumference of foot at the level	$10\frac{1}{2}''$ $10\frac{1}{2}''$	
of head of talus Bloodpressure	9½" 150/90	8½" 155/88

AETIOLOGY AND PATHOLOGY

There has been a great deal of discussion as to what is the underlying cause of hæmangiectatic hypertrophy of limbs. Parkes-Weber thinks that the primary lesion is a tumour-like hæmangiomatous overgrowth in the vascular system, which can be roughly compared to the condition of plexiform neuroma, often associated with soft tissue or even skeletal overgrowth. He does not think that this is entirely due to an increased blood supply of one-half of the body. The angiomata are not always limited to the hypertrophied side of the body, as was well demonstrated by a case of Hutchison which showed hypertrophy of the left side in addition to small capillary angiomata of the skin on the left and right side, and multiple angiomata in the liver. Kalischer suggested a vasoconstrictor paralysis as a possible explanation of the general hypertrophy of the affected Läwen in 1903 reported a case of Braun's, of typical hæmangiectatic hypertrophy, and explains the condition as a spontaneous or idiopathic progressive dilatation of the affected blood-vessels (arteries, veins and capillaries), but does not think that there is any new formation of blood-vessels.

Many French writers think that congenital syphilis may be the cause of the condition. Pautrier and Ullmo in a series of papers reported a case of a microcephalic boy of 14 with hæmangiectatic hypertrophy of the left foot. Though the Wassermann reaction was negative in this case, they thought of syphilis

as an ætiological factor and mention a case of Beatty's, a girl of 13 with hypertrophy of the right arm, dilated veins and angioma formation. She was also suffering from disseminated choroiditis, and they think that this was a case of congenital syphilis although no Wassermann test had been done. Lastly, Pardo Castello reported on a girl of 15 whose right leg was hypertrophied and who had dilated veins and capillary nævi in addition to dilated arteries in Scarpa's triangle, as was shown by arteriography. The patient's mother had a positive Wasserman reaction, but her Wasserman reaction was negative. It will therefore be seen that the evidence for congenital syphilis as a cause of the Parkes-Weber syndrome is rather

Gougerot and Filliol, describing the hæmangiectatic hypertrophy of the left hand in a man aged 23, believe that the congenital disturbance in the fætal development is probably primarily due to a lesion in the nervous system—probably decreased sympathetic vasoconstrictor tone. The increased blood supply produces an increased growth of the tissues and often a rarifaction of bone as described by Bizzozero and others. Paterson and Wyllie, whose case was a boy of seven with a hypertrophy of the right leg, observed that there was a dilatation of the vessels round the knee joint, and believe that this increased vascularity round the growing ends of the tibia and femur caused the overgrowth of these bones.

Most of the workers agree that the hypertrophy may in part at least be due to the increased blood supply. In this connection it is interesting to note the experiments which have been performed by Harris and Wright in order to determine if increase in blood supply can cause hypertrophy of tissues. examined a case of hæmangiectatic hypertrophy previously reported by Gray. This was a boy of ten whose right leg was bigger and longer than the left. It was also three degrees warmer and the arteries were felt to be distinctly larger and the pulsation greater than in the left. A thrill could be felt and a harsh continuous murmur heard over the right femoral artery. Digital obliteration of the right femoral artery caused a drop of ten beats per minute in the pulse rate. Repeating experiments by Claude Bernard, Bidder, and Stirling, they removed the right stellate ganglion in three to four weeks old kittens, measuring the growth of the bones of the fore limbs by X-rays. Though the temperature increased appreciably on the right side, the bones did not grow faster. In another experiment, conducted on young rabbits, one to two centimetres of the cervical sympathetic nerve on the right side were removed and the growth and temperature changes of the ears were measured. The temperature of the ears became between 0.8 and 2.9 degrees higher on the right side, and three rabbits out of a series of nine showed quite definite elongation of the right ear, while the remaining six showed no difference between the two sides. They deduced from these experiments that the simple increase in blood supply explains the increased growth of the soft tissues but not the bony hypertrophy, the distinction possibly resting on the sympathetic nerve distribution.

Recently several American writers who have had experience of many cases of this condition have brought forward a great deal of evidence showing that, in their cases at least, the cause of hæmangiectatic hypertrophy was a congenital arterio-venous fistula. The condition of congenital arterio-venous aneurysm was supposed to be a very rare one, and Gallander, who collected cases from the literature since John Hunter's time, could only find three cases out of a total of 447, the others being of traumatic origin.

Pemberton and Saint published in 1928 a report on a series of cases, four of which showed hypertrophy of limbs in connection with dilated veins. Thrills could be felt and systolic bruits heard over the arteries. Three of these showed an enlarged heart and increased pulse pressure in the affected limbs. All four showed nutritional disturbances of the affected limbs which necessitated ligating the arteries and veins proximal to the aneurysm. In three patients this operation did not improve the condition and the limb had to be amputated. Dean Lewis described six cases of congenital arteriovenous aneurysm, five of which occurred in the limbs and showed the same symptoms and signs as those described by Pemberton. In four, the arteries and veins proximal to the fistula were ligated and divided, but in only two was the operation entirely successful. He draws attention to the fact that the bradycardiac reaction is an excellent aid to the diagnosis of the condition. This reaction, first described by Nicoladoni in a case of congenital arterio-venous fistula, consists in applying pressure to the arteries proximal to the aneurysm; a distinct fall in the pulse rate should be detected. After the pressure is released the pulse rate should return to its previous level. By applying this test the approximate position of the aneurysm can be found. Horton, reporting on 24 cases of congenital arterious-venous aneurysms, associated with hypertrophy of limbs which occurred in the Mayo Clinic, stresses the value of the estimation of the oxygen content of the venous blood in the affected limb. In cases of arterio-venous fistulæ the venous blood returning from the limbs has an oxygen content much higher than normal. He asserts that, because previous workers had not applied this test, they had been unable to recognise that arterio-venous fistula was the cause of hæmangiectatic hypertrophy. It must be added that Pemberton, Lewis and Horton could prove the occurrence of arterio-venous fistulæ in their cases by dissection of the amputated limbs. Lastly, Blumgart and Ernstene have reported a case similar to the above. They state that congenital arteriovenous fistulæ can be recognised by the following criteria: (1) The increased pulse pressure in the affected limb, (2) the bradycardiac reaction, (3) an increased venous pressure in the affected limb, (4) a systolic thrill over the affected vessels, (5) systolic venous pulsation, and (6) an increased oxygen content in the venous blood.

Though it must be admitted that all the cases described by the American workers were undoubtedly due to congenital arterio-venous fistulæ, it does not follow that all the other cases of hæmangiectatic hypertrophy must have the same causation. This is especially true as most cases, including the one described in this paper, show none of the criteria which are supposed to be necessary for diagnosing this condition.

TREATMENT

Most of the cases of hæmangiectatic hypertrophy described in the literature did not incapacitate the patients to such an extent as to necessitate treatment. In the cases of congenital arterio-venous fistulæ various treatments have been tried, but none has been an outstanding

Pardo Castello used deep X-ray treatment without success, and, while subsequent electrodesiccation improved the condition of the vessels for two years, they gradually recurred. Lewis, reviewing the operative treatment of 27 cases of congenital aneurysm in the extremities reported in literature, states that in six of them (Letenneur, Krause, Obalinski, Ballin, Pemberton (2)) amputation had to be performed owing to repeated hæmorrhages or because the rapidly enlarging vessels destroyed the tissues. In seven cases (Gross, Israel, Eiselsberger, Reid, Perthes, Pemberton (2)) amputation of the lower limb had been necessary, chiefly because of gangrene. Only in three cases had the operation of tying and partly excising the vessels proximal to the aneurysm been followed by complete cure (Rienhoff, Reid, Lewis).

A case of hæmangiectatic hypertrophy is described in a boy of 13 who showed enlargement of the right arm and leg in connection with multiple nævi, enlarged veins and cavernous hæmangiomata. Theories as to the underlying ætiology and pathology of this condition are discussed. New vessel formation, decreased sympathetic vaso-constrictor tone, congenital syphilis and congenital arterio-venous aneurysm have been considered by different workers to play a part in the causation of the lesion. It appears that the former is an operative cause in the case described

As it is impossible to give all references of case reports of hæmangiectatic hypertrophy of limbs, readers are referred to the papers of Parkes-Weber, Dean Lewis, Kummer and Ghiso for a more complete list.

I want to express my thanks to Dr. James Maxwell for permission to publish the case and for his help and advice, and to Dr. F. Parkes-Weber for his assistance as regards the literature. I want to thank H. W. Balme for his help in preparing the paper and Mr. K. J. Randall for the photographs.

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CHRISTIAN UNION

Visit of General Sir William Dobbie

On Thursday, November 26th, we had the privilege of a visit from General Sir William Dobbie, until recently the Governor of Malta. Professor Paterson Ross kindly acted as Chairman, Matron having allowed us the use of the Nurses' Lecture Room, which was filled to capacity.

Professor Ross, in his opening remarks, stressed the privilege that was ours in having so eminent a man to visit us. He said he was sure that we should hear from General Dobbie that the secret of Malta's success lay not only in its munitions but also in those qualities of character which counted for even Professor Ross then called upon General

Dobbie to give us his lecture. General Dobbie began by telling us that he had recently come under the care of the medical profession himself, having had his appendix removed some months previously by an old Bart.'s surgeon. He was now as good as new, he said. The General said that he had spoken many times since his return on the subject of Malta from many different aspects. He proposed now to deal particularly with the medical aspect of the island's great defence. For the first months of war, their task had been comparatively easy from all points of view. France was on our side, Italy was neutral, and the control of the Mediterranean was in the hands of the Allies. It was well that it should have been so, said General Dobbie, for in those early days only four obsolete aeroplanes borrowed from the Navy could be spared for Malta, and they possessed only a very few anti-aircraft guns. But since those days, of course, the strength of the defences had been increased enor-When France fell and Italy entered the war, the Italians were continually boasting of the things they were going to do to Malta. Often they had said they were going to capture the island within two or three days. But the Maltese were made of sterner stuff than to be intimated by such threats. When the serious bombing of Malta did begin,

much improvisation of the existing medical services was necessary to deal with the increased casualties. General Dobbie said that even before the war Malta (which was the home of the Order of St. John) had a fair number of hospitals. St. Bartholomew's was the leper hospital of the island-leprosy being wellknown in Malta. The staff of this hospital in particular was always noted for its great devotion to its work. Many of the hospitals were like St.

Bartholomew's, largely confined to treatment in one branch of medicine—as the tuberculosis hospital and the big mental hospital. Since the outbreak of war, many spare beds had been prepared in the hospitals and many large buildings had been requisitioned for the same purpose—but they always hoped that there would be more Germans in these beds than Maltese! The shortage of doctors and nurses was now particularly acute, and it was very difficult to get medical supplies through to the island.

General Dobbie went on to say how severe the rationing had been in Malta. Butter was unknown, and margarine extremely scarce. There was some consolation in the plentiful supply of oranges—in fact, there were many thousands even in his own garden! General Dobbie said that as Governor he had sent—as was the annual custom—a crate of oranges to the King before he left. There were many epics which could not yet be fully told of convoys which had battled their way through to the garrison, bringing the means whereby those in Malta could

effectively visit the Germans and Italians.

On the day of the news of the entry of Italy into the war and of the imminent collapse of France, continued General Dobbie, there came to him and to the others in Malta, a feeling of a great need—the need of God. With this thought in mind, a special Order of the Day was sent from the Governor's headquarters to this effect, that with the help of Almighty God, the island would yet withstand its new perils and that those on the island should come before God to seek His help and then rely on His power to keep and guide them. And, General Dobbie said, from that time they did prove that God still does hear prayer. This was the fact that enabled Malta to hold out, coupled above all with the personal reality and companionship of the Lord Jesus Christ. This, he said, he had found throughout more than forty years of Army life, to be a very real fact— not just something for Sundays but for every day. "And it is this Person, the Lord Jesus Christ, whom I commend to you, as Saviour, Friend and Com-panion," General Dobbie concluded.

Dr. J. P. Haile proposed a vote of thanks. One of the secrets of Malta's defence that General Dobbie had not mentioned was its leader, he said, and we were left in no doubt as to what his secret was. Afterwards, General Dobbie answered many questions put

to him about Malta.

MY FIRST M.O.P.'s

By JAMES T. HAROLD

It was almost time to begin the class. So far I had only been able to collect a couple of vague dyspepsias and a fat old lady who "had pains and aches all over doctor," an inauspicious trio on which to take my first class. Then he came in. He did not walk towards me, he tottered as though pushed from behind. His arms were flexed, and there was a constant tremor of his fingers which moved over his thumbs as though he were rolling tobacco. His face was expressionless and saliva drooled from his mouth. He shook hands with me, and his arm intermittently resisted my attempts to bend his elbow. His head hung forward on his body, and he discoursed with the barest minimum of facial expression, while his eyes followed me around the room without any corresponding movements of his neck.

Here was Sydenham's plaster model brought to life, a perfect case of the Shaking Palsy, a classical example of Idiopathic Paralysis Agitans. I pretended not to appear too anxious, but grabbed the old gentleman none the less firmly by the shoulder, and took him along with me to M.O.P.'s.

The other three cases bored the students and myself equally, but I was consoled with the knowledge that to end the morning I would be able to demonstrate this obvious, but perfect teaching case. Finally the big moment arrived. "Bring in the old man," I said to one of the clerks. He tottered in, rapidly overtaking his centre of gravity until I stopped him and sat him down in front of a group of forty handsome and intelligent looking students. Anxiously they regarded his mask-like face and tremulous hands. "Now," I said, "here is the

perfect case for a spot diagnosis. What is it?" They were silent. "Perhaps you would like to see him stand," I said, and the old gentleman rose from his chair to adopt a posture of universal flexion. "Now what do you think," I said. They were still silent. Then I got him to walk, or rather, to totter across the room several times. The patient said nothing: the students said less. "Gentlemen, you disappoint me," I said, gently pushing the old gentleman with my index digit. Obligingly he gained speed and impetus until he crashed into the wall. Silently and uncomplainingly he had done his best, and so I sat him down and turned to address the doctors of the future. "Never again," I said, "will you see a case more characteristic of this condition. Now, what is this condition?" Not a soul knew. I was disappointed beyond all belief. I asked for guesses. They flowed in freely varying from Lymphadenoma to Banti's disease. Finally someone in the back row muttered something about G.P.I. The old gentleman took interest and, for the first time, opened his mouth. "G.P.I. my foot," he drawled, "you mean I.P.A." I was astounded. Had he been to another Hospital where he had been told that he was suffering from Idiopathic Paralysis Agitans? "Well," I said to the class, "you are a fine lot, waiting until the patient himself tells you the diagnosis. What does I.P.A. stand for?" Once more, complete silence. Exasperated I turned to the old gentleman and said "Well, Daddie, you will have to tell them. What does I.P.A. stand for?" His eyes turned towards me and for a second his mask-like face had vanished. "Indian Pale Ale," he said.

A CASE OF BARBITURATE POISONING TREATED WITH PICROTOXIN

By J. KENNETH IRVING

In spite of its fatal termination, particulars of the following case of barbiturate poisoning have been thought worthy of record in view of the large amount of picrotoxin used in treatment. Any apparent lack of continuity in treatment is due to the fact that the patient was in a

nursing home where there was no resident medical officer.

CASE HISTORY

The patient, a female aged 68, had been in good health, although she had recently had some lumbar fibrositis, and a mild infection of the urinary tract.

Nine months previously she had been treated in a mental hospital for a "nervous breakdown," and on two subsequent occasions had made an attempt to take her life.

Circumstantial evidence indicates that at about 8 a.m. on June 18th, 1942, she swallowed a barbituric acid compound, presumably either Medinal or Allonal or a mixture of both. Twelve hours later she was found in her room in deep coma. Her pulse and respirations were 72 and 20 respectively, the heart sounds of good quality, and the pupils normal in size. Coramine 3'4 ccs. was administered intramuscularly, and two hours later, her condition being much the same, a further similar injection was given. During the night she slept without moving, and at 10 a.m. the following morning her condition was apparently unchanged. She was then moved to a nursing home, where she was admitted at 1.15 p.m. Two further injections of Coramine were given during the afternoon. At 10.15 p.m. on June 19th, thirty-six hours after taking the drug, it was impossible to elicit any reflexes. The temperature was 101° F., the blood pressure 110 systolic and 60 diastolic, and the pupils small and equal. No physical signs of disease were found in the chest. Lumbar puncture was performed, the fluid withdrawn being normal in appearance and not under increased pressure. The pathologist's report stated that "2 mgm. of barbituric acid compound was present in 4.5 mils. of C.S.F."

Picrotoxin therapy was now started, 27 mgm. in aqueous solution being administered intravenously during the following three hours. The patient's condition seemed improved, and the temperature fell to 100° F. One ounce of castor oil in coffee was given by stomach tube. The remainder of the night was uneventful. Between midday and 2 p.m. on June 20th a further 21 mgm. of picrotoxin was administered intravenously. At 6 p.m. intensive picrotoxin therapy was started, 15 mgm. being given every 30 minutes for a period of fourteen hours. The pulse, which had shown many extra-systoles, soon became regular in rhythm and volume, and her colour, which had been dusky, improved. After 30 mgm. had been given the corneal reflex returned, the eyelids started to twitch and she was incontinent of urine and fæces. At 10.30 p.m. movements of the legs were observed, the plantar reflexes were both present and flexor, and the pupils reacted briskly to light. At 5 a.m. she moved her head from one side of the pillow to the other, her condition was much improved, and she seemed at times to be donscious. Unfortunately, however, signs of consolidation had appeared in the

Picrotoxin was discontinued during the day of June 21st, and her condition gradually worsened. The respirations were laboured and her temperature rose to 103'8°. Giant bullæ, about 1½ inches in diameter and filled with clear yellowish fluid, had appeared on the backs of the ankles and over the sacrum and tuber ischii. The same evening an intravenous drip of dextrose in saline was started and picrotoxin given in 15 mgm. doses every half hour throughout the night and following morning. Her condition once more improved, the temperature coming down quite quickly to 99°. By 2 p.m. on June 22nd 899 mgm. of picrotoxin had been given.

At 9.30 p.m. that evening, 110 hours after taking the drug, her condition was poor, consolidation of the right lung being complete. She had an unproductive cough and a marked and penetrating fector oris. Another intravenous drip was set up, and 18 mgm. of picrotoxin administered every 20 minutes. At 11 p.m. there was a sudden change in her condition, commencing with more purposeful movements of the eyes. Convulsions then started, ushered in by tonic movements of the arms and legs and followed by generalised clonic contractions, the whole attack lasting about three minutes. Respirations ceased and artificial respiration was applied. Twice for a short period the pulse was impalpable. For about five minutes after the convulsion there is no doubt that she was conscious although unable to speak: when spoken to, she turned her eyes and stared at the speaker. Within a few minutes she lapsed once more into coma, retaining her conjunctival, pupillary, palatal and plantar reflexes. Oxygen by nasal catheter was now administered. At midnight a further 3 mgm, of picrotoxin was given, but was not attended by any convulsion or further improvement. Towards morning her pulse became weak, and at 7 a.m. cyanosis of the extremities was observed although oxygen was still being given. The pupils still continued to react to light. The patient died at 8.45 a.m. on June 23rd.

The actual amount of drug taken is not known,

but seven weeks previously she had been ordered 12 tablets of Allonal for her sleeplessness, of which 1 tablet was found in her room, and four weeks previously 20 five-grain tablets of Medinal of which 8 were found. Assuming that she had consumed all the missing tablets, this would represent a total of 71 grains of barbiturate, but in view of the find-ings in the cerebro-spinal fluid, it is probably safe to assume that she had taken a good deal more, possibly as much as 100 or 150 grains. Autopsy was not performed, but the immediate cause of death was undoubtedly a pneumonia, the commonest fatal com-plication in such cases. The patient had lived for five days after taking the fatal dose, and during the last three and a half days of her life had been given 992 mgm. of picrotoxin intravenously.

COMMENT

Picrotoxin is a non-nitrogenous alkaloid derived from Anamirta Paniculata, the fruits of which, Cocculus Indicus, are the "fish berries" of commerce. It is a powerful convulsive poison, differing from strychnine in that it acts mainly on the medulla. Inactivation of the drug takes place rapidly in the body, Duff and Dille1 reporting a rapid fall in blood picrotoxin immediately after injection, a negligible amount being found in the blood after two hours. Experimentally, picrotoxin has been shown by Rosenthal² to reduce body temperature, and it is interesting to note that in this case the patient's temperature fell quite dramatically whenever picrotoxin was given. Apart from its use as an antidote to barbiturate poisoning, picrotoxin has been employed therapeutically, without any uniform degree of success, in the treatment of epilepsy, chronic alcoholism, morphine poisoning and the sleepsweats of phthisis.

The use of picrotoxin in the treatment of barbiturate poisoning was first reported in 1931 by Maloney and his associates,3 but it is interesting to note that Crichton Browne' suggested its use in the treatment of chloral hydrate poisoning as long ago as 1875. Since 1931 about fifty cases have been reported in the literature, of whom about 70% recovered, and in the remainder life was prolonged. The largest recorded dose attended by recovery is reported by Kohn, Platt and Saltman,5 who gave 671 mgm. in the space of four days. Recovery has also taken place in several cases after the administration of 200 to 300mgm. Rovenstine⁶ reports the case of a patient to whom 2134mgm. was given, who recovered sufficiently to talk on the third day, but then relapsed and died on the eighth day from hypostatic pneumonia and acute hepatitis. Anderson7 reports the occurrence in four cases of giant bullous lesions in pressure areas, similar to those observed in this case. These he attributes to an allergic manifestation of barbital, and not to picrotoxin.

Most writers are agreed that in cases of severe barbiturate intoxication, picrotoxin should be given intravenously at the rate of 30-60mgm. per hour, and that treatment should be instituted as soon as possible after the diagnosis has been made. Intravenous saline should be given to promote diuresis, and the addition of

dextrose helps to prevent acidosis. Lung complications appear to be inevitable in any case which has been in coma for more than fortyeight hours.

SUMMARY

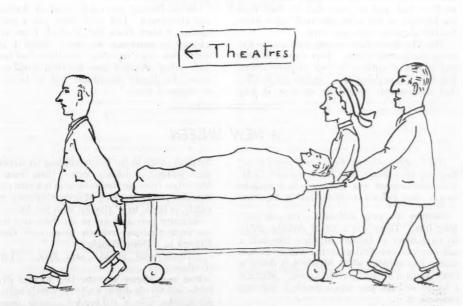
A fatal case of barbiturate poisoning is reported in which life was prolonged by the administration of 992mgm. of picrotoxin. This is believed to be the largest dose ever given in this country.

I wish to thank Dr. Gow and Dr. James Fairbrother for permission to report the case, and for their assistance in preparing this paper. REFERENCES

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- A. H. Maloney et al, J. Pharmacol, 1931, XLI., 465-482, and 1932, XLIV., 337-352.
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- III., 1938, 387-390. ⁶ E. A. Rovenstine, Am. Jr. Med. Sci., 1938,
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 7 J. P. Anderson, Ann. Int. Med., 1941, XIV., 2037-2046.



IS YOUR JOURNEY REALLY NECESSARY ?

At HILL END

Early this month the Radiogram in the Reception Hall broke down, which paralysed the activities of the Gramophone Society, interrupting their highly successful series of concerts on Sunday nights. About this time we were honoured with a visit from Miss Tina Foster, who gave us a most enjoyable Piano Recital which was a very pleasant change from the normal run of gramophone records, and we hope that she will come along again to give us another concert. In the meantime we have learnt with regret that she has returned to the hospital as a patient, we wish her a speedy recovery. This following so soon after the internal derangement of the Gramophone makes us wonder if there is not an evil spirit walking our stage in the reception hall. We sincerely hope that a similar fate does not befall another very kind lady who came along last Wednesday evening to give us an excellent piano accompaniment to our Scottish Dancing. was the last Scottish dance of the term, a Gala night. Most energetic dancing started about 9 p.m. and went on without pause until 11; by which time we just about had to swim out of the hall. We should like to thank Mrs. Patterson for one of the best evenings dancing that we have had, and we hope that we shall have the pleasure of her accompaniment again when Scottish dancing starts next term.

The Christmas show is now well on its way along the assembly lines. It is a revue written and produced entirely by our creative artists. The title, "Laughing Gas," makes me wonder that the patients would be so keen if they

knew that the genuine Laughing Gas is responsible for so much of their misery in the Surgical wards. I have still to meet a patient who takes his anæsthetic as a joke, either before or afterwards. There is a story that one patient woke up after an operation with a terrific smile across his face, opened his eyes and winked at the nurse, saying "Boy, what a dream," and then went off again to go on with it—maybe he had had a pre-view of the show!

The Choral Society is doing well with its concert which is to be performed on December 16th. Last month I said something about the unrecognizable strains of carols floating down the corridors. Since then there has been a vast improvement, some people coming into practices late have interrupted carols to announce that they sounded wonderful from outside the hall, this was often preceded by an observer from within interrupting to point out how terrible the singing was and that improvement would have to be made very quickly. Provisional plans have been drawn up to lodge the Choir outside, and the audience in the hall.

At a recent election held here K. E. Rimmington was elected to the Committee of the Hill End Bart.'s Club.

Mixed Hockey goes on as usual on Wednesday afternoons. Last week there was a match against a team from Bart.'s which I am very pleased to announce we won. Since I last wrote this news reporting that there had been only minor casualties there has been a real one, when the plastic department had to be used to restore a nose.

A NEW UNSEEN

Our readers must all have spent many hours puzzling their heads over Latin unseens. This is another unseen and although in a modern tongue, may prove equally difficult to translate.

Saturday the gang met over a coke at Joe's Juke Box. There was a lot of mahaha going on on account of because Myrtle's date took a run out powder Friday at the Candy Shop's snazzy jam session, while Myrtle was doing a Hedy Lamarr in the comfort station. Myrtle's a looloo and the guy was a meatball anyways you look at it.

All the gang was there—Eddie, Pete, Al, and a hot clasp of sugars from Phi Kappa. Honey

Svenson comes in for plenty kidding on account she's wearing a Johnny Jeep. Then there is Marie Lou from ole Kentucky who is a yum yum type and plenty convex. Maxine Schroeder, my steady, is home fixin' cookies with her Mom.

Someone puts a nickel in the Juke and that ole fruit machine certainly gives with Gene Kruppa in "Drum Boogie."

"That's solid grand," says Pete. "Let's circulate."

Pete and Honey are sure hep to that jive. Eddie and Myrtle dig it, while Al, who is having hoy-toy-toy with a red-headed campus queen whose perimeter puts you in mind of Ann Sheridan, is yelling "C'mon, you Alligators,

give!" Which leaves me on the stag line. I think, maybe, the time is ripe for pitchin' a little woo south of the Mason-Dixon, so I ease over to Marie Lou.

"Hi, Molasses! How about puttin' the show

on the road?"
"You can say that again, lambpie," she cooes, and before you can say Mugsy Spanier we're in the groove. Boy! that looloo sure is one hep-cat.

Well, me and Marie Lou are just breakin' in a pair of shoes on the down beat when a meatgrinder parks by the sidewalk outside, and in walks the puddlebuster with Maxine Schroeder who is a drum majorette in the High's brass section. This puddlebuster is the drizzlepuss that I said was a meatball anyways you look at it. The loosetooth is wearing a tuxedo and Maxine is smoothio in something dreamed up by Harpers Bazaar. Judas Priest! Is the gang interested?

"Hi, fellows, what's cookin'?" drools the

Myrtle is looking like she's fixin' to make second base.

"Hi, Myrtle," drips the drool-kind of sickly—like he just dove into a swimmin' hole full of the Dead End Kids.

"Well, cut off my legs and call me Shorty!" says Myrtle, "The Wolf comes to town."

Maxine gives me a Camel-Ad. smile.

Hi, Playmate," she says, "What are you featurin'? You look like you've just been

This is too much from a baby who is meant to be home with her Mom fixin' cookies, so I crack: "With your nerve, I'd sure hate to have a tooth pulled.

Maxine throws me her Cafe Society look and turns to the drizzle.

"Let's get on the ball, Don. I could eat anything that don't bite me first," and then they blow.

Well, patch my pantywaist! Happen I was a glass of milk, I'd curdle," says Marie Lou, Springfield Ky's gift to sophomores. "Come on, worm, squirm.'

What have I got to lose? I like my chicken southern-fried.

J. R. N.

CORRESPONDENCE

To the Editor, St. Bartholomew's Hospital Journal Dear Sir,

I was interested to read the article on "The Obstetric Case with Complications," written by Dr. H. Morris Jones in the October JOURNAL, and also the letter by Dr. V. C. Medvei, in your last publication, but feel that, taken together, they may leave your readers in some doubt as to whether pregnant diabetics commonly require more or less insulin as pregnancy proceeds to term.

In a series of 54 diabetic pregnancies recently published in the "Quarterly Journal of Medicine," R. D. Lawrence and I found that out of 37 cases on insulin at the time of conception by the third trimester 26 required more insulin, 8 showed no change, and only 3 needed a smaller dose.

From these findings it would seem that Dr. Medvei's cases should be regarded as exceptional and worth recording, not only on that account, but also as a reminder to Dr. Morris Jones that it is unwise to conclude from one case that "an increased amount of insulin is required during pregnancy." also quote cases in which the amount required after delivery was more than that required before preg-nancy, although such cases are again exceptional.

With regard to the excessive production of insulin by the foctal pancreas referred to by both your writers the literature provides much suggestive evidence in favour of this, mostly in the form of descriptions of hyperplastic islet tissue in non-surviving infants of diabetic mothers, but occasionally supported by clinical and biochemical evidence of neonatal hypoglycæmia. In this latter connection I would refer Dr. H. Morris Jones to the work of Ketteringham and Austin, from which he will dis-cover that the blood sugars of the twins he described are both above the lower limit of normal for infants of non-diabetic mothers, and therefore provide no evidence in favour of excessive insulin production by the fœtus.

Lastly, it seems to me that "Giant" babies could only be cited as evidence in support of the theory that "the fœtal pancreas produces excess insulin to counteract the effect of the mother's hyperglycamia" if their occurrence were shown regularly to be associated with a fall in maternal insulin requirement in the latter months of pregnancy, and, in spite of his two cases, I can assure Dr. Medvei that, if a large series of cases is considered, this association cannot be established. "Giant" babies in this condition are held to be the result either of uncontrolled maternal hyperglycæmia or, possibly, over-action of the anterior pituitary. Had Dr. Medvei used his "Giant" babies as an argument in favour of more careful control of the maternal diabetes during pregnancy or of Cæsarean Section at the 36th to 37th week, I should have been in complete agreement with him.

I am, yours sincerely, WILFRID OAKLEY.

149, Harley Street, W.1. November 12th, 1942. To the Editor, St. Bartholomeu's Hospital Journal

For the second time in the space of a few months we have received a diatribe from the secretary of cricket, he even goes so far as to state that his real views are unprintable. Before starting to put an alternative view I should like to say that I have no personal animosity whatsoever towards him, but his irresponsible statements have caused such a spate of cold fury in some quarters that it is time someone

told him a few facts.

There are many people in this hospital, who, although being mediocre performers are always willing to turn out provided that reasonable consideration and courtesy are shown to them. To my mind it smacks of bad taste to clarify under the term etc." those who are willing to act as "stand-ins' and who are often only notified at the very last moment—this occurred on several occasions last

That bane of a lot of Bart.'s team-the clique system-was also a considerable factor in not producing a fully representative side. A Test cricketer, who was a total abstainer, would have difficulty in maintaining his place on the side. Numerous examples could be quoted of people preferring to play for sides other than the hospital team. It is a matter of considerable regret that this unfortunate matter should receive the public airing the JOURNAL affords, but the time has come for some blunt speaking. I must once again emphasise that it is the system and not the individual tthat I am attacking.

I am, Sir, Yours faithfully,

ANTHONY.

St. Bartholomew's Hospital, Monday, November 10th.

To the Editor, St. Bartholomew's Hospital Journal In March of this year, it was decided that a memorandum on Medical Education should be prepared in St. Bartholomew's Hospital. And on November 4th the memoranda from Hill End and Bart,'s were presented to the Student Union Council.

After some discussion, it was decided to expose these two documents in the Abernethian Rooms at Bart.'s and at Hill End, and to invite criticism of them. They were accordingly left in the respective Abernethian Rooms, and were, I believe, fairly widely

Several criticisms were received of both memoranda, and at a meeting of the Student Union Council held on December 2nd, it was decided that these criticisms should be considered by the committees that had drawn up the memoranda, and that these documents, so revised, should then be taken as being reasonably representative of student opinion. It was further agreed that copies of the final memorandum should be sent to the Dean of the Medical College, and thus to the Medical College Committee for their consideration. It was further agreed that the two memoranda as presented should be fused into one document in order to prevent overlapping.

At the moment, there is an Inter-departmental Committee on Medical Schools at the Ministry of Health, which is considering the whole complex question of Medical Education. It is to this Committee that the B.M.S.A. Memorandum is to be forwarded. As the Committee at the Ministry of Health had expressly stated that they were anxious to receive memoranda prepared by representative bodies of medical students, I accordingly wrote to them saying that we had prepared a memorandum, and asking if they would like to see a copy. They replied that they would be very glad to receive 25 copies, and by the time that this appears in print these will be in their hands.

On behalf of the Students' Union Council, I would like to thank those responsible for the compilation of this weighty report, and to congratulate them on their perseverance and hard work.

D. V. BATES,

Secretary to the Students' Union. St. Bartholomew's Hospital, December 10th, 1942.

At CAMBRIDGE

On November 23rd, a general meeting of the Students' Union was held. Professor Hartridge was in the chair and about a third of the students were present. It was decided to hold three general meetings each term and it has since been arranged that the first of these shall be a business meeting and the other two meetings of the Junior Abernethian Society. It was also decided that debating, dramatic, art and musical societies be formed and the table tennis club was given official recognition. As usual, the meeting was somewhat drawn out and was still going strong at black-out, having already lasted nearly two hours; further discussion was held over until a second meeting a week later. At this meeting a tenth of the students were present and the motion was passed that, subject to our having representatives on the Council, the Medical College in Cambridge would join the University of London Union.

After starting the season with a string of easy victories, the Soccer club has recently had a few setbacks which were mainly due to nearly half the team being incapacitated by injuries of one sort or another. However, the Inter-Collegiate League matches are not yet over and, despite all, the Bart.'s team is still in the first three with two games to go. Burns and Mc-Clusky are to be congratulated for playing for London University.

A dance is to be held on February 4th; the committee responsible for its organisation is under the guidance of Dr. Metten and it is hoped that this dance will be an even greater success than the one he ran two Christmasses

M. D. S.

SPORTS NEWS RUGGER

v. King's College Hospital, at Chislehurst, 7th November. Won 17-0.

November. Won 17—0.

For the first time we fielded a full set of outsides who showed greatly improved form against not very good opposition. The grass was very wet, making the ball heavy and hard to hold. We attacked from the start and produced several good movements, notably a scissors by Hunt and Davey, but it was from loose play that we scored, Stephen and Stephens going over for two unconverted tries. In second half there were many excellent rushes, and from one of these Wigglesworth scored. Pitman broke away and with Corbett's support scored a try, which Gibson converted, the only other score being a penalty goal.

Team.—J. H. Gibson; P. H. Davey, M. R. Hunt, R. F. Jones, P. R. Hawkes; C. S. M. Stephen, A. B. Wood; R. G. Mann, A. Jones, R. L. Hall, A. R. Anderson, J. R. Moffat, A. R. Corbett, J. P. Stephens. v. Cambridge University. Away. 11th November. Won 13—3.

Whether it was due to the large and noisy crowd or the lengthy train journey I don't know, but the team played an inspired game. The Varsity as usual set a very hot pace, but we managed to go as fast and even faster at times. Hawkes was cutting through very well inside his opposite number and at the third attempt he scored a try, which Gibson converted; for the rest of the half we made most of the play but could not score again.

Setting off in the second half at an even faster pace we kept the Varsity in their 25 for some time, and then Stephen wormed his way over from a scrum, Gibson converting. Very shortly after this R. F. Jones scored as a result of a good three-quarter movement. Gibson failed to convert.

The Varsity came back strong, and we had a bad fifteen minutes of frenzied defence, but their only score was a penalty goal, one of our forwards being much too tired to get off the ball. In the last few minutes we again attacked but without scoring. A most encouraging game. A vote of thanks to the large crowd who came and cheered us on.

Team.—Gibson; Davey, Hunt, Pitman, Jones; Hawkes, Stephen; Wood, Mann, Jones, Hall, Anderson, Stephens, Corbett, Wigglesworth.

v. Royal New Zealand Air Force. Chislehurst. 14th November. Won 13-3.

The R.A.F. had some difficulty with their navigation, so that the game started rather late. Repeating the tactics successful at Cambridge we went off at a fast pace, and after a little open play Gibson came up from full back to score far out after about five people had handled; he was unable to convert. Though the forwards were getting plenty of the ball most movements broke down as it was rather greasy, on one of the rare occasions that it got to the wing Jones ran very strongly to score a try, which Gibson converted. One of our dropped passes was picked up by their centre threequarter, who scored an unconverted try.

They attacked very strongly in the second half, producing some very good forward rushes and several dangerous runs by Grant on the wing. By counter rushes we returned to their 25 and Wigglesworth scored a try, Gibson converting. Play became very scrappy and no scoring resulted.

very scrappy and no scoring resulted.

Team.—Gibson; Davey, Hunt, Pitman, Jones;
Hawkes, Stephen; Wood, Mann, Jones, Anderson,
Wigglesworth, Stephens, Corbett, Moffat.

v. Aldershot Services. Chislehurst. 21st November. Won 22-0.

To start with we could not get the ball quickly enough, and so our movements were smothered; eventually Hawkes forced himself over, Gibson failing to convert, a feat he repeated several times from various angles. The services made one strong attack without scoring. In the second half, playing with the wind, we improved tremendously. We got the ball quickly and smoothly, and both wings looked dangerous; but it was Pitman who scored after running half the length of the field, Gibson converting. We then had a patch of really grand forward play, resulting in Stephens scoring three remarkable tries. Just before the end another rush gave Wood a try, which Hawkes converted.

Team.—Gibson; Davey, Hunt, Pitman, Jones; Hawkes, Stephen; Wood, Mann, Jones, Anderson, Hall, Stephens, Wigglesworth, Moffat.

v. London Hospital, Chislehurst. 28th November. Won 33-0.

This was very nearly a complete rout. The backs and forwards combined well, especially late in second half. The following scored:—Tries: Hunt, Pitman 2, Moffat, Jones, Stephens. Drop Goals: Hunt, Hawkes. Penalty: Hawkes. Goals: Hawkes, Gibson.

Team.—Gibson; Davey, Hunt, Pitman, Jones; Hawkes, Stephen; Wood, Mann, Jones, Anderson, Moore, Stephens, Wigglesworth, Moffat.

v. Coventry. Away. 5th December. Lost 29—3. A chapter of accidents. Illness and a united hospitals match combined to reduce us to a glorified "A" XV, to add to our troubles after fifteen minutes Hawkes was injured and limped about on the wing. The opposition had a typical Midlands pack, heavy and experienced. As a result we seldom got the ball. However, we managed to keep them down to 8 points in the first half. In the second half they ran away from us, there seemed to be 20 of them on the field. The forwards struggled well under Jones' leadership, but the backs were overrun. Just before no side we had some sort of a movement from which Gibson scored a try, which he failed to convert.

Team.—Livingstone; Davey, Hunt, Gibson, Jones; Hawkes, Thomas; Wood, Mann, Rimmington, Anderson, Moore, Jones, Marcroft, Moffat.

At CAMBRIDGE

At the beginning of the term there were a large number of enthusiasts and the prospects for a successful season were fairly bright. It was arranged that, if possible, three teams should be run.

that, if possible, three teams should be run.

The 1st XV started off quite well with two or three wins. Most of the players looked as though they knew how to play football. They visited Hill End, and after giving quite a convincing display, were beaten just on time. From that day they have slowly deteriorated to the present level; nearly all the College sides have proved superior, and a pack of old women could probably run circles round them.

The 2nd XV enjoyed their games when a full team was put into the field. All credit must go to their secretary, F. P. Wallis, who has had an uphill task trying to find fixtures for them and chasing after people when the 1st XV has commandeered half the side.

ASSOCIATION FOOTBALL

v. Selwyn College. Saturday, November 7th. Won 5-1.

The first few minutes of this game showed the Bart.'s team dazzled by several lightning movements by the opponents, mainly because of a brilliant righthalf who was responsible for every Selwyn attack, which, as the game progressed, became fewer and fewer.

We settled down fairly quickly, however, and opened the scoring after ten minutes, when Burns scored with a first-time cross shot which their goalie just failed to grasp. Not long afterwards he scored again by getting to the ball first in a goal-mouth scrimmage.

By this time the play was mainly in the Selwyn half, and the whole team was combining extremely well; Blackman and Mangan both shot inches out-side the posts, and 30 minutes after the start Goodrich neatly deflected a pass from Burns past the goalie, thus giving us a 3-0 lead.

McCluskey, as usual playing as a roving inside-left, was doing really excellent work and was rewarded with a fine goal when he dribbled past three defenders and sent in a long hard shot which their goalie never saw. This 4-0 lead was temporarily unsettled, however, when the Selwyn right-half tore through our defence and placed a brilliant shot past Pine in goal.

The second half saw clever football: it was all attack in this half, and only because of their heavy strong defence did they keep the ball out of their goal. With Mangan feeding our wing men and Murley lobbing the ball into the goal mouth they had many lucky escapes.

Pine in goal played safely during their infrequent attacks, most of which were efficiently dealt with by Jordan and Murley. Mangan playing well up, combined with Blackman, Burns and McCluskey, these four being mainly responsible for our decisive win.

Team.—Pine; Team.—Pine; Xavier, Jordan; Gai, Murley, Mangan; Burns, Blackman, Goodrich, McCluskey, Whiteley.

BOAT CLUB

At the beginning of this term a meeting was held to elect club officers for the present season. The response was very satisfactory and much better than last year when we only had sufficient men to form a first racing eight. This year we started practices early on; two eights were formed and a third is now being selected.

Originally, the first eight was to take part in the time races held in November, but owing to lack of training and other minor inconveniences, this was not possible. Latterly there have been several outings, and we are now settling down to a programme of intensive training so that at least two eights can be entered for the Lent races.

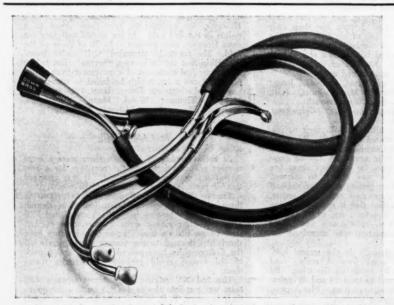
Many people have been sculling this term, and Dr. Town has offered a prize for a sculling competition, to be held in the Summer term.

A new set of oars is urgently needed so that we can have two eights on the river at the same time, and it is hoped that some funds will be forthcoming from the Students' Union for this purpose.

We are sorry that, due to pressure of work, our Captain of Boats, G. B. Chamberlain, is resigning, and we are very grateful both to Dr. Town and to Dr. Fawns (of London Hospital) for the time and trouble they have expended in coaching us.

C. M. WHITEHEAD-EVANS

(Hon. Sec.).



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